REMARKS/ARGUMENT

Claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41-44, 53, 55-58, 66, 86, 88-89, 91-92, 95-96, and 98-114 are pending and were examined in this application.

In this paper, dependent claims 22, 29, 31, 32, 53, 66, 86, 88, and 89 are amended without prejudice or disclaimer. No new claims are added. Applicants reserve the right to pursue the subject matter removed by amendment in future applications. With the entry of this amendment, claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41-44, 53, 55-58, 66, 86, 88-89, 91-92, 95-96, and 98-114 remain pending.

Claim 22 is amended to recite labeled charged carrier molecules. Support for this amendment is found in at least page 32, lines 9-31 of the specification. Claims 29, 31, and 32 are amended to provide antecedent support for the recited "separation media." Support for a separation media in the separation channel is at least found in original claim 28 and pages 44-46 of the specification.

Similarly, claims 86, 88, and 89 are amended to provide antecedent support for the recited "concentration media." Support for a concentration media in the concentration channel is found at least in original claim 85 and pages 73-74 of the specification.

Claim 53 is modified to simplify the claim language. Claim 66 is amended to provide antecedent support for the limitation recited therein. Support for the amendment is found at least in original claim 62.

As noted, all of the above amendments either are supported by the specification and/or the original claims or are of a minor clerical nature. Accordingly, the amendments add no new matter. Applicants respectfully request reconsideration of the pending claims in the application.

I. General Remarks on Office Action

Applicants gratefully acknowledge that in the current Office Action, the Office withdrew all ten rejections made in the previous Office Action (mailed October 14, 2009). Thus, all of the ten separate rejections made in the prior Office Action in sections 7-16 under 35 U.S.C. § 103 were withdrawn.

In the current Office Action, however, the Office also rejected the pending claims under 35 U.S.C. § 103, as allegedly being obvious over three combinations of the following references: WO 02/082083 to Kawabata et al. ("Kawabata"), U.S. Patent 5,611,903 to Janssens et al. ("Janssens"), Kaniansky et al. in Analytical Chemistry, Vol. 72, p. 3596 (2000) ("Kaniansky"), Brown et al. in J. Biol. Chem., Vol. 269, p. 26801 (1994) ("Brown"), EP 1061370 A2 to Hosokawa et al. ("Hosokawa"), and Kautz et al. in J. Am. Chem. Soc., Vol. 123, p. 3159-3160 (2001) ("Kautz"). The Kautz reference is the only reference newly applied by the Office.

Specifically, claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 53, 55-58, 86, 88-89, 91-92, 95, 101-102, and 105-106 were rejected over Kawabata, in view of Janssens, Kaniansky, and Kautz;

claim 66 was rejected over Kawabata, in view of Janssens, Kaniansky, and Kautz, further in view of Brown; and

claims 10, 23-26, 38-39, 41-42, 96, 98-100, 103-104, and 108-114 were rejected over Kawabata, in view of Janssens, Kaniansky, and Kautz, further in view of Hosokawa.

II. Claim Rejections Under 35 U.S.C. § 103 - Obviousness

A. Office Action, Section 7 at page 3: Claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 53, 55-58, 86, 88-89, 91-92, 95, 101-102, and 105-106

Claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 53, 55-58, 86, 88-89, 91-92, 95, 101-102, and 105-106 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kawabata, in view of Janssens, Kaniansky, and Kautz. Applicants respectfully traverse.

Applicants respectfully submit that, as set forth below in detail, at least three references, Kawabata, Kautz, and Janssens, do not teach or suggest the claimed elements as alleged by the Office Action. Furthermore, the combination of at least Janssens and Kautz is improper because the references would be rendered inoperative for their intended purpose. Therefore, the combination of references lacks at least some of the claimed elements and cannot support a prima facie case of obviousness. Because all the claim limitations are not taught or otherwise suggested by the prior art, the claimed invention as a whole would not have been obvious to one of skill in the art.

The Office Action states that, with respect to claim 1, Kawabata teaches a method of detecting an analyte that involves forming a complex between an analyte and a nucleic acid chain-binding affinity substance-marker. Office Action at 4. Allegedly, Kawabata further teaches the separation of the complex from the unbound substance-marker. *Id.* The Office Action then states that Kawabata's sample containing the analyte and substance-marker may further comprise a nuclease inhibitor, one of which is said to be heparin. The Office Action then concludes that heparin is a polyanion that "reduces the interferences of the nuclease which might be present in the solution." *Id.* Apparently, the Office infers that this teaching meets the limitation of a "first polyanion" according to the claims. The Office Action does acknowledge,

however, that Kawabata does not teach concentrating the analyte, and therefore cannot teach a concentration step in the presence of a "second polyanion." *Id.* at 4-5. The Office Action further alleges that Kawabata teaches a separation method, but acknowledges that Kawabata does not teach a "third polyanion." *Id.* at 5.

The Office Action references Kaniansky for teaching a concentration pretreatment step, but acknowledges that Kaniansky does not teach the presence of a "second polyanion" in this step. *Id.* at 6. The Office Action next alleges, however, that "it was well known in the art that polyanions could be used" in such a step. *Id.* To support this, the Office Action presents Kautz for the teaching that the walls of a capillary "need to coated with polyvinyl alcohol" to minimize electroosmotic flow (EOF), which would degrade the analyte bands' boundaries. *Id.* at 6-7, 13.

Finally, the Office Action states that Janssens teaches adding a polyanion during an electrophoresis separation step. *Id.* at 7. Further, it is said that Janssens teaches that the use of a polyanion allows for higher velocities and shorter migration times. Thus, "because migration times would be shorter," the Office alleges that the polyanion would reduce interferences, and would thus be a "third polyanion." *Id.*

Based on the above in relevant part, the Office Action alleges that the combination of these references teaches all the limitations of claim 1. *Id.* Applicants respectfully traverse.

Kawabata

The rejection relies on Kawabata's disclosure of using heparin to inhibit enzymatic degradation by nucleases for allegedly teaching a "first polyanion." According to Kawabata, heparin is one example of a nuclease inhibitor (the others are small-molecule chelators, such as EGTA or EDTA) that can be added to a sample to protect nucleic acid chains. *See* Kawabata at [0191].

However, the use of an inhibitor, such as heparin, by Kawabata does not "reduce interference with separating the complex" as recited by the claims. As recited, the function of the first, second, and third polyanions is to "reduce interference with separating the complex." Some of the types of interferences contemplated include the formation of non-specifically binding complexes, creation of noisy backgrounds, creation of false peaks and the like due to the presence of "interfering constituents that bind non-specifically to assay components." *See, e.g.*, specification at 2. Thus, the polyanions function to avoid distortions to electrophoretic separations, which would result in a loss of accuracy or sensitivity. *Id.*

As taught by Kawabata, the nuclease inhibitors (heparin being one example) function to preserve the existence of a nucleic acid chain substance. In other words, according to Kawabata, nucleases that would otherwise destroy the nucleic acid chains are to be inhibited. Thus, Kawabata neither teaches nor suggests the use of inhibitors to prevent distortions of a separation due to non-specifically bound constitutes. Instead, Kawabata simply teaches that an inhibitor is useful to prevent the degradation of nucleic acid chains. Furthermore, the examples provided by Kawabata do not use an inhibitor (including heparin), thus there is no disclosure in the reference that might teach or suggest any other role for the inhibitors.

It should also be recognized that Kawabata does not teach or suggest that there may be a problem, *i.e.*, interference to an electrophoretic separation from sample constituents, which needs to be solved. The particular problem solved by Kawabata is unrelated to the recitations in the claims. Kawabata states that inhibitors are only appropriate "when there is a possibility of the existence of a nuclease or nucleases" in the sample. Kawabata at [0191]. Thus, Kawabata does not suggest using inhibitors where no nucleases are expected—the addition of an inhibitor is optional according to Kawabata.

Thus, Applicants respectfully assert that Kawabata does not teach or suggest the use of a "first polyanion" to reduce interference with separating a complex as recited in the claims. Kawabata addresses an unrelated problem and simply proposes a means for preventing a specific degradation reaction. Kawabata neither recognizes, teaches, nor suggests a "first polyanion" that is useful for reducing non-specific binding by sample constituents which distort electrophoretic separations. Accordingly, one of skill in the art would not find the claimed invention obvious in view of Kawabata because Kawabata does not teach or suggest a "first polyanion," as alleged. For at least this reason, Applicants respectfully request that the rejection be withdrawn.

Kautz

The Office Action relies on Kautz to support the assertion that it was well known in the art that polyanions could be used in a concentration channel, *i.e.*, that Kautz teaches a "second polyanion." Office Action at 6, 13. According to the Office Action, Kautz teaches coating a capillary with polyvinyl alcohol to prevent degradation of the boundaries between the analyte bands. *Id.* at 13. Applicants respectfully assert that (1) polyvinyl alcohol is not a polyanion, and, in any event, (2) preventing degradation of analyte bands does not teach or suggest reducing interference with separating a complex.

Polyvinyl alcohol is a neutral polymer. The alcohol functional group is defined by a hydroxy moiety (-OH), which is neutral at all relevant solution conditions. The structural formula of polyvinyl alcohol can be found in the Sigma-Aldrich Catalog. (Sigma-Aldrich Corp. specializes in organic and inorganic chemicals for chemical synthesis, medicinal chemistry, and materials science. The company markets over 100,000 different chemicals. *See, e.g.*, www.sigmaaldrich.com/customer-service/about-us.html.) A copy of the web site's catalog page for polyvinyl is provided as an attachment to this paper.

As the catalog entry shows, polyvinyl alcohol is composed of a hydrocarbon "backbone" which has side groups attached to every other carbon atom that are represented by "OH." The "OH" groups are hydroxy groups, and these groups are not anionic. Thus, the polyvinyl alcohol compound disclosed by Kautz is not a polyanion.

In addition, the teaching by Kautz that polyvinyl alcohol-coated capillaries minimize electroosmotic flow (EOF) is unrelated to the function of the "second polyanion" as recited in the claims. Degradation of the boundary of analyte bands simply results in a separation having a reduced resolution. The cause of the loss of resolution is the flow patterns arising from EOF. This is similar to the teaching found in Kaniansky (Kaniansky explains that conducting capillary electrophoresis experiments without EOF yields the highest reproducibility and reliability of quantitative CE results. *See id.* at p. 3599, right column, first paragraph), but this is not related to the reduction of interference arising from non-specific interactions between sample constituents and the analyte complex as recited.

Applicants submit that Kautz does not teach or suggest the concentration of analytes in the presence of a polyanion, nor, therefore, could the reference teach or suggest the use of polyanions to reduce interference with separating the analyte(s). Accordingly, one of skill in the art would not find the claimed invention obviousness in view of Kautz because Kautz does not teach or suggest the limitation of a second polyanion or reduced interference as alleged in the Office Action. For at least this reason, Applicants respectfully request that the rejection be withdrawn.

Janssens

The Office Action relies on Janssens for allegedly teaching separating a complex in the presence of a "third polyanion" and thereby reducing inference with separating the complex.

According to the Office Action, Janssens teaches "adding a polyanion to a capillary buffer in a capillary electrophoresis detection method," and that "the use of a polyanion in a buffer allows for higher velocities and shorter migration times of complexes being separated." *Id.* at 7; *see also id.* at 13. From this, the Office concludes, "therefore this third polyanion would reduce the interferences because the migration times would be shorter." *Id.* at 7.

Applicants respectfully assert that Janssens does not teach or suggest a "third polyanion," that is, a polyanion that would reduce interference with separating the complex, as recited in claims 1, 39, and 42, and all claims depending therefrom.

Janssens does not teach at all the recited limitation, the "reduction of interference" in separations caused by noise constituents in a sample. Janssens teaches methods for controlling EOF which result in better reproducibility. *See* Janssens, col. 2, lines 41-45; col. 7, lines 18-28; col. 16, lines 50-55; col. 19, lines 43-54; col. 21, lines 1-14, 47-49. Janssens also teaches that, under some conditions, increased separation resolutions can be achieved in shorter times. *Id.*, col. 7, line 46 – col. 8, line 6. The Office Action alleges that shorter migration times "allows for better elution of the analyte." Office Action at 13. However, no rationale is provided for why a shorter migration time teaches the "reduced interference" between an analyte and other constituents. Applicants assert that non-specific binding interactions between noise constituents and the analyte would have been established prior to the separation step, and thus regardless of the length of time required for the separation, the separation profile of the analyte would be distorted due to the interference.

Whereas the claimed invention is concerned with reducing interference from "noise constituents" that derive from the sample, Janssens does not even suggest such a problem exists. Instead, Janssens is concerned with "the direct stabilization of the EOF of a capillary." Janssens,

col. 7, lines 22-23. In presenting the problem to be solved, Janssens teaches "a constant electroosmotic mobility (EOF) during analyses is necessary to obtain reliable analytical results." *Id.* at col. 2, lines 41-43. Janssens neither teaches nor suggests that there even is interference with the assay due to other sample constituents, let alone that, as the subject invention discloses, a polyanion can block interference with the separation assay "by interacting with sample constituents that interfere with the assay." Specification at 15, lines 30-31.

Also, as Applicants have stated before, Janssens does not disclose the separation of complexes but only of non-complexed analytes. *See, e.g.*, Janssens, col. 23, lines 21-23; col. 26, lines 64-65; col. 31, lines 35-40, 55-58; col. 32, lines 49-51; col. 33, lines 1-3, 58-62. All of the samples that Janssens uses for illustrating the methods, such as aniline and benzene derivatives and even blood or serum, are analyzed in terms of the separation achieved for each single, uncomplexed component of the sample.

Applicants submit that Janssens does not teach or suggest the separation of complexed analyte species, nor the use of polyanions to reduce interference with separating such analyte(s). Accordingly, one of skill in the art would not find the claimed invention obviousness in view of Janssens because Janssens does not teach or suggest the limitation of reduced interference as alleged in the Office Action. For at least this reason, Applicants respectfully request that the rejection be withdrawn.

It Is Improper to Combine Janssens and Kautz

The teachings of Janssens and Kautz are at odds with one another and would lead one of skill in the art away from combining them with each other.

Janssens teaches that the addition of both a polycation and a polyanion result in a stable and more reproducible EOF, and that the addition of both charged polymers is necessary.

Janssens, col. 18, lines 15-22; col. 19, lines 3-16; col. 21, lines 1-7 (note that the "initiator of Janssens is a polymer with positive charges, *see* col. 10, lines 45-54). In contrast, Kautz teaches the use of a neutral polymer for "minimizing" EOF. Kautz, p. 3159, right column. The motives provided by Janssens and Kautz are contradictory, as one seeks to stabilize EOF while the other teaches the need to minimize, *i.e.*, suppress, EOF. It is well established that the proposed modification cannot render the prior art unsuited for its intended purpose, or that it cannot change the principle of operation of a reference. *See* MPEP § 2143.01.V-VI. Here, an attempt to combine Janssens and Kautz would do just that because their teachings are mutually exclusive.

The combination of these references cannot support a prima facie case of obviousness as it would be improper to combine these references as presented by the Office Action to achieve the claimed invention.

Applicants submit that pending claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 53, 55-58, 86, 88-89, 91-92, 95, 101-102, and 105-106 are not obvious, the rejection under § 103 should be withdrawn, and the claims should be allowed for the reasons set forth above.

B. Office Action, Section 8 at page 13: Claim 66

Claim 66 was rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kawabata, Janssens, Kaniansky, and Kautz as applied to claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 53, 55-58, 86, 88-89, 91-92, 95, 101-102, and 105-106, further in view of Brown. Applicants respectfully traverse.

If an independent claim is nonobvious under 35 U.S.C. § 103(a), then any claim depending therefrom is nonobvious. *See* MPEP 2143.03. Claim 66 depends from claim 1, which, as noted, is not rendered obvious by the combination of Kawabata, Janssens, Kaniansky,

and Kautz. The teaching of Brown does not remedy the deficiencies of Kawabata, Janssens, Kaniansky, and Kautz with respect to claim 1. The Office Action applies Brown for allegedly teaching a mobility shift assay using phosphorothioate-modified oligonucleotides. Office Action at 14. Brown does not teach or suggest, however, providing a first, second, or third polyanion as claimed, the elements also not provided in Kawabata, Janssens, Kaniansky, and Kautz as explained above.

Kawabata, Janssens, Kaniansky, Kautz, and Brown, alone or combination, do not teach or suggest all the limitations of independent claim 1, from which claim 66 depends. Therefore these references, considered as a whole, do not render the claim obvious. For at least this reason, Applicants respectfully request that the rejection of claim 66 under § 103 be withdrawn.

C. Office Action, Section 9 at page 15: Claims 10, 23-26, 38-39, 41-42, 96, 98-100, 103-104, and 108-114

Claims 10, 23-26, 38-39, 41-42, 96, 98-100, 103-104, and 108-114 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kawabata, Janssens, Kaniansky, and Kautz as applied to claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 53, 55-58, 86, 88-89, 91-92, 95, 101-102, and 105-106, further in view of Hosokawa. Applicants respectfully traverse.

First, Applicants respectfully note that claim 107, although pending, was not addressed in the Office Action. Based on the dependency and the subject matter of claim 107, Applicants assume herein solely for the purpose of filing a fully responsive reply that the Office would apply the analysis of Section 9 to this claim as well.

If an independent claim is nonobvious under 35 U.S.C. § 103(a), then any claim depending therefrom is nonobvious. *See* MPEP 2143.03. Claims 10, 23-26, 38, 96, 103-104, and 107-108 depend (ultimately) from claim 1, which, as noted, is not rendered obvious by the

combination of Kawabata, Janssens, Kaniansky, and Kautz. The teaching of Hosokawa does not remedy the deficiencies of Kawabata, Janssens, Kaniansky, and Kautz with respect to claim 1. The Office Action applies Hosokawa for allegedly teaching a contacting step wherein one or more non-conjugated affinity molecules have affinity against the analyte. Office Action at 15.

Hosokawa is not noted, however, to teach any of a first, second, or third polyanion as claimed. Independent claims 39 and 42, and claims 41, 98-100, and 109-114, which depend therefrom, also incorporate the limitations of claim 1 reciting a first, second, or third polyanion, which, as explained above, are not found in Kawabata, Janssens, Kaniansky, and Kautz.

Kawabata, Janssens, Kaniansky, Kautz, and Hosokawa, alone or combination, do not teach or suggest all the limitations of independent claims 1, 39, or 42 from which claims 10, 23-26, 39, 41, 96, 98-100, 103-104, and 107-114 depend. Therefore these references, considered as a whole, do not render these claims obvious. For at least this reason, Applicants respectfully request that the rejection of claims 10, 23-26, 38-39, 41-42, 96, 98-100, 103-104, and 107-114 under § 103 be withdrawn.

III. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully requests that the amendments and remarks place claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41-44, 53, 55-58, 66, 86, 88-89, 91-92, 95-96, and 98-114 in condition for allowance.

Applicants submit that the claimed invention is not obvious in view of the prior art references cited against this application. Applicants therefore request the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
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Dated: January 4, 2011

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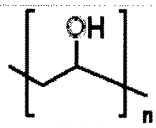
Attachment: Sigma-Aldrich Catalog, Poly(vinylalcohol)

Product Image



1 of 1

P1763 Poly(vinyl alcohol)

Sigma **Fully hydrolyzed**

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Price and Availability

Product Number	Availability	Your Price USD	Quantity	Actions
P1763-250G	In Stock *details...* Ships on 12/12/10	34.00		
P1763-1KG	In Stock *details...* Ships on 12/12/10	103.00		

CAS Number: 9002-89-5

Linear Formula: $[-CH_2CHOH-]_n$

MDL number: MFCD00081922

Customers Also Purchased

P8136

No Image Available

Poly(vinyl alcohol)
87-90% hydrolyzed, average mol wt 30,000-70,000

Details Related Products References Reviews

Properties

viscosity 11-14 cP, 4 % in H_2O(20 °C)(lit.)

solubility H_2O: soluble (hot)

Safety

Personal Protective Equipment Eyeshields, Gloves, type N95 (US), type P1 (EN143) respirator filter

WGK Germany 1

RTECS TR8100000

Flash Point(F) >235.4 °F

Flash Point(C) >113 °C